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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,813	02/02/2007	Robert Huber	HUBR-1295	5848

24972 7590 06/23/2009
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EXAMINER	
DAHLE, CHUN WU	
ART UNIT	PAPER NUMBER
1644	
MAIL DATE	DELIVERY MODE
06/23/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,813	HUBER ET AL.	
	Examiner	Art Unit	
	CHUN DAHLE	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *54-111* is/are pending in the application.

4a) Of the above claim(s) *54-69,73,74,76,77,88-91,94-105 and 107-111* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *70-72,75,78-87,92,93 and 106* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/25/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of Group IV (drawn to antibodies that bind FcγRIIb) and species of non-blocking antibodies that target sequence of FcγRIIb of SEQ ID NO:2 in the reply, filed on April 6, 2009, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-53 have been canceled.

Claims 54-111 have been added and are pending.

It is noted that claim 93 recites a diagnostic kit comprising antibody or CDE peptide. Claim 93 is considered as elected invention only to the extend of the antibody.

Claims 54-69, 73, 74, 76, 77, 88-91, 94-105, and 107-111 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

Claims 70-72, 75, 78-87, 92, 93, and 106 are currently under consideration as they read on the elected invention of non-blocking antibodies that bind FcγRIIb of SEQ ID NO:2.

2. Applicant's IDS, filed on May 25, 2006, is acknowledged. The IDS has not been considered because applicant fails to provide copies of the foreign patents and publications cited. Applicant is reminded that in accordance with 37 CFR 1.98, the following items must be included a legible copy of (i) each foreign patent; (ii) each publication or that portion which caused it to be listed, other than US patents and US patent application publications unless required by the Office. In addition, the two Non Patent Literature Documents, CA and CB, listed on IDS are not in compliance with 37

CFR 1.98 because the documents are not identified with publisher, author (if any), title, relevant pages of the publication, date, and place of publication (see 37 CFR 1.98(b)(5)).

3. Claim 70 is objected to for being dependent upon withdrawn claim 54. For examination purposes, claim 70 is read as a substance that specifically binds to the peptide or polypeptide comprising conformationally discriminating epitope (CDE).

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 70-72, 75, 78-87, 92, 93, and 106 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 70-72, 75, 78-87, 92, 93, and 106 recite "An antibody or fragment or derivative thereof" and claims 83 and 84 recite an antibody that is a polypeptide carrying "one or more" CDRs as part of the invention.

The specification does not provide sufficient guidance or working examples of "An antibody or fragment or derivative thereof" or an antibody that is a polypeptide carrying less than six CDRs.

The specification discloses methods of generating antibody by immunizing mouse with specific peptides from FcγRIIa or FcγRIIb. However, the specification does not provide any guidance regarding how to make antibody derivatives that would share the same function as the original antibody. It is unpredictable with respect to altering amino acid sequence of an antibody variable region and maintaining the antibody function. It is

well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (PNAS 1982 Vol 79 page 1979). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function.

While there are some publications which acknowledge that CDR3 is important, the conformations of other CDRs as well as framework residues influence binding.

MacCallum et al. (J. Mol. Biol. (1996) 262, 732-745) analyzed many different antibodies for interactions with antigen and state that although CDR3 of the heavy and light chain dominate, a number of residues outside the standard CDR definitions make antigen contacts (see page 733, right col) and non-contacting residues within the CDRs coincide with residues as important in defining canonical backbone conformations (see page 735, left col.).

Pascalis et al. (The Journal of Immunology (2002) 169, 3076-3084) demonstrate that grafting of the CDRs into a human framework was performed by grafting CDR residues and maintaining framework residues that were deemed essential for preserving

the structural integrity of the antigen binding site (see page 3079, right col.). Although abbreviated CDR residues were used in the constructs, some residues in all 6 CDRs were used for the constructs (see page 3080, left col.).

The fact that not just one CDR is essential for antigen binding or maintaining the conformation of the antigen binding site, is underscored by *Casset et al. (BBRC(2003) 307, 198-205)*, which constructed a peptide mimetic of an anti-CD4 monoclonal antibody binding site by rational design and the peptide was designed with 27 residues formed by residues from 5 CDRs (see entire document). Casset et al. also states that although CDR H3 is at the center of most if not all antigen interactions, clearly other CDRs play an important role in the recognition process (page 199, left col.) and this is demonstrated in this work by using all CDRs except L2 and additionally using a framework residue located just before the H3 (see page 202, left col.).

Vajdos et al. (JMB (2002) 320, 415-428) additionally state that antigen binding is primarily mediated by the CDRs more highly conserved framework segments which connect the CDRs are mainly involved in supporting the CDR loop conformations and in some cases framework residues also contact antigen (page 416, left col.).

Holm et al (Molecular Immunology (2007) 44, 1075-1084) describes the mapping of an anti-cytokeratin antibody where although residues in the CDR3 of the heavy chain were involved in antigen binding unexpectedly a residue in CDR2 of the light chain was also involved (abstract).

Further, the claims encompass antibody "derivative" or antibody "part". However, the specification fails to disclose how to derive such antibody or antibody part and maintaining the binding specificity to FcγRIIb. For example, the SEQ ID NO:9 is 100% identical to antibody variable light chain disclosed in Frenken et al. (WO 00/05389); however, the instant antibody binds to FcγRIIb; while the prior art antibody has antigen specificity to azo-dye RR6 (e.g. see page 23 and Example III on pages 32-40

and SEQ ID NO:9 alignment attached to this Office Action). Similarly, the instant SEQ ID NO:11 is 100% identical to the heavy chain variable region of the mouse monoclonal antibody 1A7 that is an anti-idiotypic antibody produced with an antibody specific for ganglioside GD2 disclosed in Chatterjee et al. (US 2005/0287148) (e.g. see Figure 3B and SEQ ID NO:11 alignment attached to this Office Action). Therefore, the instant SEQ ID NOs: 9 and 11 must be paired together to have the claimed function of binding FcγRIIB. As such, the instant claims reciting only one heavy chain variable region or light chain variable region are not enabled to one of skill in the art because such single chain antibody would not have the claimed antigen specificity.

Furthermore, a fragment of an antibody can be the heavy chain or any one of the constant regions (CH1-3) and also may be the hinge region. However, the language also reads on small amino acid sequences which are incomplete regions of the constant region of the antibody. There is no support in the specification for linking the variable region to any or all of the myriad "fragments" which are encompassed within this language. One of skill in the art would neither expect nor predict the appropriate functioning of the antibody as broadly as is claimed. It is suggested that the specific portion of the human constant region, which the variable region is covalently linked to, be explicitly recited within the claim (e.g. antigen binding fragment thereof) or this language be removed completely in order to obviate this rejection.

Therefore, in view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall

> have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 70-72, 75, 78-87, 92, 93, and 106 are rejected under 35 U.S.C. 102(e) as being anticipated by Koenig et al. (US Patent 7,425,620) as evidenced by the CDRs location of variable light region of mAbGB3 disclosed in Figure 5 of the instant specification.

Koenig et al. teach a monoclonal antibody that specifically binds native human FcγRIIb which is endogenously expressed and present on surface of a cell with higher affinity than FcγRIIa (e.g. see column 9-16). Koenig et al. further teach a species of said antibody, 3H7, whose light chain variable region is 92.3% identical in amino acid sequence to the instant SEQ ID NO:5; the instant SEQ ID NO:5 shares at least the same CDR1 sequence to the prior art light chain variable region of 3H7 (see CDR1 location of the instant SEQ ID NO:5 on Figure 5 of the specification as-filed).

Furthermore, Koenig et al. teach:

A) anti- FcγRIIb antibody that is IgG, IgE, IgM, or IgA (e.g. see column 16),

B) anti- FcγRIIb antibody that is single chain, Fab fragment, F(ab)2 fragment, scFv fragment (e.g. see column 16), bispecific or trispecific antibody (e.g. see column 27),

C) pharmaceutical composition comprising said antibody (e.g. see column 13 and claims 10-13),

D) anti- FcγRIIb antibody that is modified in the Fc region for alteration of glycosylation or amino acid substitutions for enhanced binding affinity towards FcγRs (e.g. see column 32-33),

E) a kit comprising antibody that can be used for diagnosing autoimmune diseases (e.g. see columns 5-6 and 103).

Given that the instant claims (e.g. claim 87) recite a part of the antibody sequence rather than full length of the variable regions, the prior art antibody that is 92.3% identical to the instant SEQ ID NO:5 would read onto the instant claims.

Moreover, given that the prior art antibody has the same structure and antigen specificity as the instant antibody, it would be an inherent property for the prior art antibody to be able to bind a CDE of FcγRIIb.

Therefore, the reference teachings anticipate the claimed invention.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Dahle whose telephone number is 571-272-8142. The examiner can normally be reached on 8:30-5:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Ram Shukla can be reached 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Chun Dahle/
Examiner, Art Unit 1644